REMARKS

Claim 1, 16 and 17 were amended to strike out reference to prodrugs. Claim 1 was also amended, deleting the substituent "X" and its definition from the Claim, since "C-X" was no longer part of Claim 1. Claim 5 was cancelled, since it further narrowed Claims 1 and 2 based upon the definition of X, which was no longer part of the amended Claim 1. In an effort to expedite prosecution, Claim 1 was also amended to limit the definition of R^2. Similarly, Claim 4 was amended to restrict the scope of R^2 as defined in Claim 1. Likewise, Claim 8 was amended to narrow the scope of the claim to be commensurate to that of Claim 1. New Claims 18-22 were added. Support for these claims are found in the original Claim 1.

Applicants reserve the right to file, without waiver or prejudice, a divisional or continuation application directed to subject matter cancelled herein.

35 U.S.C. § 103(a) Rejection of Claims 1-8 and 15-17

The Examiner rejected Claims 1-8 and 15-17 under 35 U.S.C. § 103(a) as being obvious over Fisher et al. (U.S. 5,077,290). The Examiner contends that Claims 1-8, 15 and 16 are obvious wherein A is N; B is CY and Y is NH_2; and Z is H. The Examiner further states that Claim 16 is rendered obvious, because it is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification. The Examiner claims that the motivation to make the claimed compounds derives from the expectation that structurally similar compounds possess similar activity. Finally, the Examiner simply states that Claim 17 is obvious, where A is CX and X is NH_2 and Z is H.

Applicants traverse the rejection of Claims 1-4, 6-8 and 15-17 and respectfully submit that the Examiner failed to make a prima facie case of obviousness.

In establishing the prima facie case, the Examiner engages in an analysis of four Graham factors. With respect to the first factor – the scope and content of the prior art – the Examiner correctly notes that Fisher teaches compounds useful as growth promotants, broncodilators, antidepressants and antiobesity agents. The Examiner also provides a structural formula of the compounds claimed by Fisher, but only depicts three of the possible five variations for which "Het" is defined. Accordingly, the scope of Fisher is broader than that depicted by the Examiner.

With respect to the second factor – ascertaining the differences between the prior art and the claims at issue – the Examiner simply states that the difference between Fisher and "the instantly claimed compounds is that the *Fisher et al.* invention, is in scope. Both the instant invention and the prior art are drawn to morpholine substituted pyridines. The difference is that the instant invention is a genus of the prior art." Office Action, pg 6, par. 1.

Applicants disagree with the Examiner's characterization of the scope of Applicants' invention, with respect to that of Fisher et al. Notwithstanding, given that Applicants amended Claim 1 and Claim 8, narrowing the definition of the substituent R^2 to $(C_1\text{-}C_6)$alkyl, the scope of Applicants' claims clearly do not encompass those of Fisher nor *vice versa*. In particular, Fisher et al. is limited to those compounds wherein both R^1 and R^2 are hydrogen. Accordingly, the scope of Applicants' invention differs from that of Fisher et al.

With respect to the third and fourth Graham factors, the Examiner states that the pertinent art is classified as medicinal chemistry and drug discovery. Furthermore, in support of the *prima facie* case of obviousness, the Examiner contends that one of ordinary skill in the art would be motivated to make and use the instant claimed invention, because Fisher et al. teaches the preferred embodiments of the instant invention. In particular, the Examiner contends that the motivation to make the claimed compounds derive from the expectation that structurally similar compounds are generally expected to have similar properties and have similar utilities.

The Examiner further contends that the *prima facie* case for obviousness is derived from the preferred compounds and preferred variable substituents. In particular, the Examiner notes that the amino substituted pyridine (formula "a") is a preferred genus, as well as the lower alkyl is a preferred substituent, "R" on the morpholine ring. According to the Examiner, therefore, the teachings of Fisher et al would motivate one skilled in the art to make and use the instant compounds and compositions with the expectation that they would both have the same pharmokinetic effect. The Examiner concludes that Applicants' invention is obvious where A is nitrogen, B is CY and Y is NH_2 and Z is hydrogen. The Examiner also concludes that Claim 16 is obvious, because the substitution of methyl for hydrogen on a known compound is well-known. The motivation, according to the Examiner, is the expectation that structurally similar compounds would possess similar activity.

Applicants respectfully disagree with the Examiner's conclusion that Fisher et al. motivates one skilled in the art to arrive at Applicants' invention. According to the MPEP, the Examiner must determine whether one of ordinary skill in the art would be motivated to make the claimed invention as a whole, *i.e.*, to select the claimed species or subgenus from the disclosed prior art genus. MPEP § 2144.08 (II., A., 4).

First, Applicants submit that the invention as amended and claimed by Applicants is not a subgenus or species of Fisher et al. Fisher et al. is only directed to a non-substituted morpholine ring at the equivalent R^1 and R^2 positions of Applicants morpholine ring. Nor, as amended is Fisher et al. a sub-genus of the present application. In contrast, Applicants' invention is directed to R^1 and/or R^2 substituted morpholine compounds, wherein both R^1 or R^2

cannot be hydrogen. Accordingly, Applicants' invention not only does not fall within the scope of Fisher et al.

Furthermore, Applicants submit that Fisher et al. does not teach nor suggest the addition of a substituent – namely R^1 and/or R^2 – to the morpholine ring. Fisher et al. is only directed to non-substituted morpholine compounds at the equivalent R^1 and R^2 positions. Accordingly, there is no teaching, suggestion nor motivation to attach *e.g.* a methyl group, as claimed in Claim 16, to the morpholine ring.

"[A] *prima facie* casie of unpatentability requires that the teachings of the prior art *suggest the claimed compounds* to a person of ordinary skill in the art." Id. at 2100-154 (emphasis added)(citing Deuel, 51 F.3d at 1557). Furthermore, the prior art must provide one of ordinary skill in the art the motivation to make the proposed molecular modifications needed to arrive at the claimed compound. In re Lalu, 747 F.2d 703, 705 (Fed. Cir. 1984).

As discussed above, Fisher et al. does not provide the motivation or suggestion to arrive at Applicants claimed compounds. The Examiner contends that Fisher et al. motivates one skilled in the art, because Fisher et al teaches preferred compounds. In doing so, the Examiner points out that preferred compounds are those having a "formula a", as the HET substituent and wherein N-lower alkyl is a preferred "R" substitution on the morpholine ring.

In evaluating a prior art, the "reference must be considered not only for what it expressly teaches, but also for what it fairly suggests." In re Baird, 16 F.3d 380; 29 USPQ.2d 1550 (Fed. Cir. 1994). The Examiner ignores the express teachings of Fisher et al, as well as what the reference suggests. In particular, the Examiner overlooks the most preferred teaching wherein R is tert-butyl or 1,1-dimethylpropyl, that is optionally substituted with optionally substituted phenyl or indolyl. Col. 3, lines 1-7. Fisher et al. also sets forth at Table I specific examples of preferred examples – none of which are N-propyl substituted on the morpholine ring. Accordingly, Fisher et al., not only provides no motivation to arrive at Applicants' invention, it teaches away from Applicants' invention on multiple levels, because the disclosure indicates a *preference leading away* from Applicants' claimed inventions. See Id. at 383 (noting that the prior art reference discloses preferred substituents that were more complex than that claimed and, therefore, does not teach or suggest the selection of the claimed substituent).

First, one skilled in the art would believe, from the teachings of Fisher et al., that both R^1 and R^2 should be hydrogen – not that a hydrogen could be substituted with a methyl. Second, Fisher et al. explicity teaches preferred N-alkyl substituents that are preferably –branched lower alkyls (col. 2, lines 55-68), *e.g. t*-butyl or 1,1-dimethylpropyl, optionally substituted with optionally substituted phenyl or indolyl, as well as those substituents depicted in Table I. One skilled in the art, from the teachings and suggestions of Fisher et al., would not expect that N-

alkyl could be a simple propyl chain. Instead, one skilled in the art would expect that a more sterically hindered group is required at N-alkyl on the morpholine ring.

When relying on a modification of prior art, it is incumbent upon the examiner to identify some suggestion to make the modification. In re May, 104 F.3d 1339, 1342 (Fed. Cir. 1997). As discussed above, there is no suggestion in Fisher et al. to add a R^1 and/or R^2 substituent, as claimed by Applicants. Furthermore, the preferred teachings of Fisher et al. direct one skilled in the art to branched alkyl groups that are optionally substituted.

At best – which Applicants do not concede – this is a situation where it may be "obvious to try" to make modifications to the compounds disclosed in Fisher et al. Fisher et al.'s general disclosure, while it may "pique the scientist's curiosity, such that investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued." In re Eli Lilly and Co., 902 F.2d 943, 945 (Fed. Cir. 1990)(citing In re O'Farrell, 853 F.2d 894, 903-04 (Fed. Cir. 1988)). Obvious to try, however, is not the standard for establishing a prima facie case of obviousness.

Because Applicants' invention, as amended, is not encompassed within the invention of Fisher et al and there is no teaching, motivation or suggestion to make the modifications claimed by Applicants, the Examiner has failed to establish a prima facie case of obviousness. Applicants respectfully request that the Examiner reconsider the rejection of Claims 1-4, 6-8, and 16-17.

35 U.S.C. § 112(1st Par.) Rejection of Claims 1, 16 and 17

Applicants believe the rejection to Claims 1, 16 and 17 is rendered moot, in light of Applicants' amendments. Accordingly, Applicants respectfully request withdrawal of the rejection to these claims.

CONCLUSION

Having addressed all points and concerns raised by the Examiner, Applicants respectfully request an early and favorable action in this application.

Respectfully submitted,

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